SEQUENCE LISTING

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<110> MCINNES, CAMPBELL
     MCLACHLAN, JANICE
     MEZNA, MOKDAD
     FISCHER, PETER
<120> METHOD FOR IDENTIFYING INHIBITORS USING A HOMOLOGY
      MODEL OF POLO-LIKE KINASE 1
<130> CCI-067US
<140> 10/579,006
<141> 2006-05-11
<150> PCT/GB04/004762
<151> 2004-11-12
<150> GB 0326396.9
<151> 2003-11-12
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<170> PatentIn Ver. 3.3
<210> 1
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      peptide
Met Ser Tyr Tyr His His His His His Gly Met Ala Ser Asp Asp
Asp Asp Lys
<210> 2
<211> 6
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<213> Artificial Sequence
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      His tag
<400> 2
His His His His His
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2
<210> 3
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     peptide
<400> 3
Arg Arg Glu Glu Glu Thr Glu Glu Glu
<210> 4
<211> 603
<212> PRT
<213> Homo sapiens
<400> 4
Met Ser Ala Ala Val Thr Ala Gly Lys Leu Ala Arg Ala Pro Ala Asp
Pro Gly Lys Ala Gly Val Pro Gly Val Ala Pro Gly Ala Pro Ala
             20
                                 25
Ala Ala Pro Pro Ala Lys Glu Ile Pro Glu Val Leu Val Asp Pro Arg
Ser Arg Arg Arg Tyr Val Arg Gly Arg Phe Leu Gly Lys Gly Gly Phe
                        55
Ala Lys Cys Phe Glu Ile Ser Asp Ala Asp Thr Lys Glu Val Phe Ala
Gly Lys Ile Val Pro Lys Ser Leu Leu Lys Pro His Gln Arg Glu
Lys Met Ser Met Glu Ile Ser Ile His Arg Ser Leu Ala His Gln His
Val Val Gly Phe His Gly Phe Phe Glu Asp Asn Asp Phe Val Phe Val
Val Leu Glu Leu Cys Arg Arg Ser Leu Leu Glu Leu His Lys Arg
    130
                        135
                                            140
Arg Lys Ala Leu Thr Glu Pro Glu Ala Arg Tyr Tyr Leu Arg Gln Ile
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Val Leu Gly Cys Gln Tyr Leu His Arg Asn Arg Val Ile His Arg Asp

Leu Lys Leu Gly Asn Leu Phe Leu Asn Glu Asp Leu Glu Val Lys Ile 185

Gly Asp Phe Gly Leu Ala Thr Lys Val Glu Tyr Asp Gly Glu Arg Lys 200

195

- Lys Thr Leu Cys Gly Thr Pro Asn Tyr Ile Ala Pro Glu Val Leu Ser 210 215 220
- Lys Lys Gly His Ser Phe Glu Val Asp Val Trp Ser Ile Gly Cys Ile 225 230 235 240
- Met Tyr Thr Leu Leu Val Gly Lys Pro Pro Phe Glu Thr Ser Cys Leu
 245 250 255
- Lys Glu Thr Tyr Leu Arg Ile Lys Lys Asn Glu Tyr Ser Ile Pro Lys
 260 265 270
- His Ile Asn Pro Val Ala Ala Ser Leu Ile Gln Lys Met Leu Gln Thr 275 280 285
- Asp Pro Thr Ala Arg Pro Thr Ile Asn Glu Leu Leu Asn Asp Glu Phe 290 295 300
- Phe Thr Ser Gly Tyr Ile Pro Ala Arg Leu Pro Ile Thr Cys Leu Thr 305 310 315 320
- Ile Pro Pro Arg Phe Ser Ile Ala Pro Ser Ser Leu Asp Pro Ser Asn 325 330 335
- Arg Lys Pro Leu Thr Val Leu Asn Lys Gly Leu Glu Asn Pro Leu Pro 340 345 350
- Glu Arg Pro Arg Glu Lys Glu Glu Pro Val Val Arg Glu Thr Gly Glu
 355 360 365
- Val Val Asp Cys His Leu Ser Asp Met Leu Gln Gln Leu His Ser Val 370 375 380
- Asn Ala Ser Lys Pro Ser Glu Arg Gly Leu Val Arg Gln Glu Glu Ala 385 390 395 400
- Glu Asp Pro Ala Cys Ile Pro Ile Phe Trp Val Ser Lys Trp Val Asp 405 410 415
- Tyr Ser Asp Lys Tyr Gly Leu Gly Tyr Gln Leu Cys Asp Asn Ser Val 420 425 430
- Gly Val Leu Phe Asn Asp Ser Thr Arg Leu Ile Leu Tyr Asn Asp Gly
 435 440 445
- Asp Ser Leu Gln Tyr Ile Glu Arg Asp Gly Thr Glu Ser Tyr Leu Thr 450 455 460
- Val Ser Ser His Pro Asn Ser Leu Met Lys Lys Ile Thr Leu Leu Lys 465 470 475 480
- Tyr Phe Arg Asn Tyr Met Ser Glu His Leu Leu Lys Ala Gly Ala Asn 485 490 495
- Ile Thr Pro Arg Glu Gly Asp Glu Leu Ala Arg Leu Pro Tyr Leu Arg 500 505 510

Thr Trp Phe Arg Thr Arg Ser Ala Ile Ile Leu His Leu Ser Asn Gly 515 520 525

Ser Val Gln Ile Asn Phe Phe Gln Asp His Thr Lys Leu Ile Leu Cys 530 540

Pro Leu Met Ala Ala Val Thr Tyr Ile Asp Glu Lys Arg Asp Phe Arg 545 550 555 560

Thr Tyr Arg Leu Ser Leu Leu Glu Glu Tyr Gly Cys Cys Lys Glu Leu 565 570 575

Ala Ser Arg Leu Arg Tyr Ala Arg Thr Met Val Asp Lys Leu Leu Ser 580 590

Ser Arg Ser Ala Ser Asn Arg Leu Lys Ala Ser 595 600

<210> 5

<211> 685

<212> PRT

<213> Homo sapiens

<400> 5

Met Glu Leu Leu Arg Thr Ile Thr Tyr Gln Pro Ala Ala Ser Thr Lys

1 10 15

Met Cys Glu Gln Ala Leu Gly Lys Gly Cys Gly Ala Asp Ser Lys Lys 20 25 30

Lys Arg Pro Pro Gln Pro Pro Glu Glu Ser Gln Pro Pro Gln Ser Gln 35 40 45

Ala Gln Val Pro Pro Ala Ala Pro His His His His His Ser His 50 55 60

Ser Gly Pro Glu Ile Ser Arg Ile Ile Val Asp Pro Thr Thr Gly Lys 65 70 75 80

Arg Tyr Cys Arg Gly Lys Val Leu Gly Lys Gly Gly Phe Ala Lys Cys 85 90 95

Tyr Glu Met Thr Asp Leu Thr Asn Asn Lys Val Tyr Ala Ala Lys Ile 100 \$105\$

Ile Pro His Ser Arg Val Ala Lys Pro His Gln Arg Glu Lys Ile Asp 115 120 125

Lys Glu Ile Glu Leu His Arg Ile Leu His His Lys His Val Val Gln 130 135 140

Tyr Cys Ser Arg Arg Ser Met Ala His Ile Leu Lys Ala Arg Lys Val 165 170 175

- Leu Thr Glu Pro Glu Val Arg Tyr Tyr Leu Arg Gln Ile Val Ser Gly
 180 185 190
- Leu Lys Tyr Leu His Glu Glu Glu Ile Leu His Arg Asp Leu Lys Leu
 195 200 205
- Gly Asn Phe Phe Ile Asn Glu Ala Met Glu Leu Lys Val Gly Asp Phe 210 225 220
- Gly Leu Ala Ala Arg Leu Glu Pro Leu Glu His Arg Arg Arg Thr Ile 225 230 235 240
- Cys Gly Thr Pro Asn Tyr Leu Ser Pro Glu Val Leu Asn Lys Gln Gly 245 250 255
- His Gly Cys Glu Ser Asp Ile Trp Ala Leu Gly Cys Val Met Tyr Thr 260 265 270
- Met Leu Gly Arg Pro Pro Phe Glu Thr Thr Asn Leu Lys Glu Thr 275 280 285
- Tyr Arg Cys Ile Arg Glu Ala Arg Tyr Thr Met Pro Ser Ser Leu Leu 290 295 300
- Ala Pro Ala Lys His Leu Ile Ala Ser Met Leu Ser Lys Asn Pro Glu 305 310 315 320
- Asp Arg Pro Ser Leu Asp Asp Ile Ile Arg His Asp Phe Phe Leu Gln 325 330 335
- Gly Phe Thr Pro Asp Arg Leu Ser Ser Ser Cys Cys His Thr Val Pro
- Asp Phe His Leu Ser Ser Pro Ala Lys Asn Phe Phe Lys Lys Ala Ala 355 360 365
- Ala Ala Leu Phe Gly Gly Lys Lys Asp Lys Ala Arg Tyr Ile Asp Thr 370 375 380
- His Asn Arg Val Ser Lys Glu Asp Glu Asp Ile Tyr Lys Leu Arg His 385 390 395 400
- Asp Leu Lys Lys Thr Ser Ile Thr Gln Gln Pro Ser Lys His Arg Thr 405 410 415
- Asp Glu Glu Leu Gln Pro Pro Thr Thr Thr Val Ala Arg Ser Gly Thr
 420 425 430
- Pro Ala Val Glu Asn Lys Gln Gln Ile Gly Asp Ala Ile Arg Met Ile 435 440 . 445
- Val Arg Gly Thr Leu Gly Ser Cys Ser Ser Ser Ser Glu Cys Leu Glu
 450 455 460
- Asp Ser Thr Met Gly Ser Val Ala Asp Thr Val Ala Arg Val Leu Arg 465 470 475 480

Gly Cys Leu Glu Asn Met Pro Glu Ala Asp Cys Ile Pro Lys Glu Gln 485 490 495

Leu Ser Thr Ser Phe Gln Trp Val Thr Lys Trp Val Asp Tyr Ser Asn 500 505 510

Lys Tyr Gly Phe Gly Tyr Gln Leu Ser Asp His Thr Val Gly Val Leu 515 520 525

Phe Asn Asn Gly Ala His Met Ser Leu Leu Pro Asp Lys Lys Thr Val 530 535 540

His Tyr Tyr Ala Glu Leu Gly Gln Cys Ser Val Phe Pro Ala Thr Asp 545 550 555

Ala Pro Glu Gln Phe Ile Ser Gln Val Thr Val Leu Lys Tyr Phe Ser 565 570 575

His Tyr Met Glu Glu Asn Leu Met Asp Gly Gly Asp Leu Pro Ser Val 580 585 590

Thr Asp Ile Arg Arg Pro Arg Leu Tyr Leu Leu Gln Trp Leu Lys Ser 595 600 605

Asp Lys Ala Leu Met Met Leu Phe Asn Asp Gly Thr Phe Gln Val Asn 610 615 620

Phe Tyr His Asp His Thr Lys Ile Ile Cys Ser Gln Asn Glu Glu 625 630 635 640

Tyr Leu Leu Thr Tyr Ile Asn Glu Asp Arg Ile Ser Thr Thr Phe Arg 645 650 655

Leu Thr Thr Leu Leu Met Ser Gly Cys Ser Ser Glu Leu Lys Asn Arg
660 665 670

Met Glu Tyr Ala Leu Asn Met Leu Leu Gln Arg Cys Asn 675 680 685

<210> 6

<211> 646

<212> PRT

<213> Homo sapiens

<400> 6

Met Glu Pro Ala Ala Gly Phe Leu Ser Pro Arg Pro Phe Gln Arg Thr
1 5 10 15

Ala Ala Ala Thr Ala Pro Pro Ala Gly Pro Gly Pro Pro Pro Ser Ala 20 25 30

Leu Arg Gly Pro Glu Leu Glu Met Leu Ala Gly Leu Pro Thr Ser Asp $35 \hspace{1cm} 40 \hspace{1cm} 45$

Pro Gly Arg Leu Ile Thr Asp Pro Arg Ser Gly Arg Thr Tyr Leu Lys 50 55 60

Gly Arg Leu Leu Gly Lys Gly Gly Phe Ala Arg Cys Tyr Glu Ala Thr 65 Asp Thr Glu Thr Gly Ser Ala Tyr Ala Val Lys Val Ile Pro Gln Ser Arg Val Val Lys Pro His Gln Arg Glu Lys Ile Leu Asn Glu Ile Glu Leu His Arg Asp Leu Gln His Arg His Ile Val Arg Phe Ser His His 120 Phe Glu Asp Ala Asp Asn Ile Tyr Ile Phe Leu Glu Leu Cys Ser Arg Lys Ser Leu Ala His Ile Trp Lys Ala Arg His Thr Leu Leu Glu Pro Glu Val Arg Tyr Tyr Leu Arg Gln Ile Leu Ser Gly Leu Lys Tyr Leu His Gln Arg Gly Ile Leu His Arg Asp Leu Lys Leu Gly Asn Phe Phe 180 185 Ile Thr Glu Asn Met Glu Leu Lys Val Gly Asp Phe Gly Leu Ala Ala Arg Leu Glu Pro Pro Glu Gln Arg Lys Lys Thr Ile Cys Gly Thr Pro Asn Tyr Val Ala Pro Glu Val Leu Leu Arg Gln Gly His Gly Pro Glu Ala Asp Val Trp Ser Leu Gly Cys Val Met Tyr Thr Leu Leu Cys Gly 250 Ser Pro Pro Phe Glu Thr Ala Asp Leu Lys Glu Thr Tyr Arg Cys Ile Lys Gln Val His Tyr Thr Leu Pro Ala Ser Leu Ser Leu Pro Ala Arg Gln Leu Leu Ala Ala Ile Leu Arg Ala Ser Pro Arg Asp Arg Pro Ser 290 295 300 Ile Asp Gln Ile Leu Arg His Asp Phe Phe Thr Lys Gly Tyr Thr Pro Asp Arg Leu Pro Ile Ser Ser Cys Val Thr Val Pro Asp Leu Thr Pro

Pro Asn Pro Ala Arg Ser Leu Phe Ala Lys Val Thr Lys Ser Leu Phe 340 345 350

325

Val Arg Lys Lys Ser Lys Asn His Ala Gln Glu Arg Asp Glu Val 355 360 365

- Ser Gly Leu Val Ser Gly Leu Met Arg Thr Ser Val Gly His Gln Asp 370 380
- Ala Arg Pro Glu Ala Pro Ala Ala Ser Gly Pro Ala Pro Val Ser Leu 385 390 395 400
- Val Glu Thr Ala Pro Glu Asp Ser Ser Pro Arg Gly Thr Leu Ala Ser 405 410 415
- Ser Gly His Gly Phe Glu Glu Gly Leu Thr Val Ala Thr Val Val Glu 420 425 430
- Ser Ala Leu Cys Ala Leu Arg Asn Cys Ile Ala Phe Met Pro Pro Ala 435 440 445
- Glu Gln Asn Pro Ala Pro Leu Ala Gln Pro Glu Pro Leu Val Trp Phe
 450 455 460
- Ser Glu Trp Val Gly Phe Ser Asn Lys Phe Gly Phe Gly Tyr Gln Leu 465 470 475 480
- Ser Ser Arg Arg Val Ala Val Leu Phe Asn Asp Gly Thr His Met Ala 485 490 495
- Leu Ser Ala Asn Arg Lys Thr Val His Tyr Asn Pro Thr Ser Thr Lys 500 505 510
- His Phe Ser Phe Ser Val Gly Ala Val Arg Arg Ala Leu Gln Pro Gln 515 520 525
- Leu Gly Ile Leu Arg Tyr Phe Ala Ser Tyr Met Glu Gln His Leu Met 530 535 540
- Lys Gly Gly Asp Leu Pro Ser Val Glu Glu Val Glu Val Pro Ala Pro 545 550 555 560
- Pro Leu Leu Gln Trp Val Lys Thr Asp Gln Ala Leu Leu Met Leu 565 570 575
- Phe Ser Asp Gly Thr Val Gln Val Asn Phe Tyr Gly Asp His Thr Lys 580 585 590
- Leu Ile Leu Ser Gly Trp Glu Pro Leu Leu Val Thr Phe Val Ala Arg 595 600 605
- Asn Arg Ser Ala Cys Thr Tyr Leu Ala Ser His Leu Arg Gln Leu Gly 610 620
- Cys Ser Pro Asp Leu Arg Gln Arg Leu Arg Tyr Ala Leu Arg Leu 625 630 635 640

Arg Asp Arg Ser Pro Ala 645

- <210> 7
- <211> 326
- <212> PRT
- <213> Homo sapiens
- <400> 7
- Met Ser Ala Ala Val Thr Ala Gly Lys Leu Ala Arg Ala Pro Ala Asp 1 5 10 15
- Pro Gly Lys Ala Gly Val Pro Gly Val Ala Ala Pro Gly Ala Pro Ala 20 25 30
- Ala Ala Pro Pro Ala Lys Glu Ile Pro Glu Val Leu Val Asp Pro Arg 35 40 45
- Ser Arg Arg Tyr Val Arg Gly Arg Phe Leu Gly Lys Gly Gly Phe 50 55 60
- Ala Lys Cys Phe Glu Ile Ser Asp Ala Asp Thr Lys Glu Val Phe Ala 65 70 75 80
- Gly Lys Ile Val Pro Lys Ser Leu Leu Leu Lys Pro His Gln Arg Glu 85 90 95
- Lys Met Ser Met Glu Ile Ser Ile His Arg Ser Leu Ala His Gln His
 100 105 110
- Val Val Gly Phe His Gly Phe Phe Glu Asp Asn Asp Phe Val Phe Val 115 120 125
- Val Leu Glu Leu Cys Arg Arg Arg Ser Leu Leu Glu Leu His Lys Arg 130 135 140
- Arg Lys Ala Leu Thr Glu Pro Glu Ala Arg Tyr Tyr Leu Arg Gln Ile 145 150 155 160
- Val Leu Gly Cys Gln Tyr Leu His Arg Asn Arg Val Ile His Arg Asp 165 170 175
- Leu Lys Leu Gly Asn Leu Phe Leu Asn Glu Asp Leu Glu Val Lys Ile 180 185 190
- Gly Asp Phe Gly Leu Ala Thr Lys Val Glu Tyr Asp Gly Glu Arg Lys 195 200 205
- Lys Thr Leu Cys Gly Thr Pro Asn Tyr Ile Ala Pro Glu Val Leu Ser 210 225
- Lys Lys Gly His Ser Phe Glu Val Asp Val Trp Ser Ile Gly Cys Ile 225 230 235 240
- Met Tyr Thr Leu Leu Val Gly Lys Pro Pro Phe Glu Thr Ser Cys Leu 245 250 255
- Lys Glu Thr Tyr Leu Arg Ile Lys Lys Asn Glu Tyr Ser Ile Pro Lys 260 265 270

His Ile Asn Pro Val Ala Ala Ser Leu Ile Gln Lys Met Leu Gln Thr 275 280 285

Asp Pro Thr Ala Arg Pro Thr Ile Asn Glu Leu Leu Asn Asp Glu Phe 290 295 300

Phe Thr Ser Gly Tyr Ile Pro Ala Arg Leu Pro Ile Thr Cys Leu Thr 305 310 315 320

Ile Pro Pro Arg Phe Ser 325

<210> 8

<211> 320

<212> PRT

<213> Homo sapiens

<400> 8

Met Gly Asn Ala Ala Ala Lys Lys Gly Ser Glu Gln Glu Ser Val 1 5 10 15

Lys Glu Phe Leu Ala Lys Ala Lys Glu Asp Phe Leu Lys Lys Trp Glu 20 25 30

Ser Pro Ala Gln Asn Thr Ala His Leu Asp Gln Phe Glu Arg Ile Lys

Thr Leu Gly Thr Gly Ser Phe Gly Arg Val Met Leu Val Lys His Lys 50 55 60

Glu Thr Gly Asn His Tyr Ala Met Lys Ile Leu Asp Lys Gln Lys Val 65 70 75 80

Val Lys Leu Lys Gln Ile Glu His Thr Leu Asn Glu Lys Arg Ile Leu 85 90 95

Gln Ala Val Asn Phe Pro Phe Leu Val Lys Leu Glu Phe Ser Phe Lys
100 105 110

Asp Asn Ser Asn Leu Tyr Met Val Met Glu Tyr Val Pro Gly Glu 115 120 125

Met Phe Ser His Leu Arg Arg Ile Gly Arg Phe Ser Glu Pro His Ala 130 135 140

Arg Phe Tyr Ala Ala Gln Ile Val Leu Thr Phe Glu Tyr Leu His Ser 145 150 155 160

Leu Asp Leu Ile Tyr Arg Asp Leu Lys Pro Glu Asn Leu Leu Ile Asp 165 170 175

Gln Gln Gly Tyr Ile Gln Val Thr Asp Phe Gly Phe Ala Lys Arg Val 180 185 190

Lys Gly Arg Thr Trp Thr Leu Cys Gly Thr Pro Glu Tyr Leu Ala Pro 195 200 205

- Glu Ile Ile Leu Ser Lys Gly Tyr Asn Lys Ala Val Asp Trp Trp Ala 210 215 220
- Leu Gly Val Leu Ile Tyr Glu Met Ala Ala Gly Tyr Pro Pro Phe Phe 225 230 235 240
- Ala Asp Gln Pro Ile Gln Ile Tyr Glu Lys Ile Val Ser Gly Lys Val 245 250 255
- Arg Phe Pro Ser His Phe Ser Ser Asp Leu Lys Asp Leu Leu Arg Asn 260 265 270
- Leu Leu Gln Val Asp Leu Thr Lys Arg Phe Gly Asn Leu Lys Asn Gly 275 280 285
- Val Asn Asp Ile Lys Asn His Lys Trp Phe Ala Thr Thr Asp Trp Ile 290 295 300
- Ala Ile Tyr Gln Arg Lys Val Glu Ala Pro Phe Ile Pro Lys Phe Lys 305 310 315 320